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(mean+SEM) of IL-10 was produced in the supernatants of CD83<sup>+</sup> mDC2 (n=4). The term "substantially increased IL-10 production," "substantially increase in production of IL-10," "substantially increased production of IL-10," or "substantially enhanced production of IL-10" in reference to mature mDC2 IL-10 production refers to a substantial increase or substantial enhancement in mature mDC2 IL-10 production relative to the mature mDC1 IL-10 production, and typically refers to a mature mDC2 IL-10 production ranging from at least about 60% to about 100% greater, at least about 70% to about 100% greater, at least about 80% to about 100% greater, at least about 90% to about 100% greater, at least about 95% to about 100% greater, at least about 96% to about 100% greater, at least about 97% to about 99% greater, or at least about 97% to about 98% greater than mature mDC1 IL-10 production.

Page 60, line 25:

EXAMPLE 7. TRANSFECTION EFFICIENCIES OF MDC2 AND MDC1

IN THE CLAIMS:

Please amend claims 1, 2, 5-7, 10, 11, 13, 17-20, 23-25, 27-35, 37, 39-42, 44, 46, 48-50, 52-57, 60-61, 63, 65, and 68 as indicated below without prejudice to subsequent renewal in their original form. Please cancel claims 36, 43, and 69 without prejudice to subsequent renewal in their original form. Please add new claims 70-78 as follows. For ease of reference and convenience, unamended claims are included below in small type.

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1. (Amended) A method of producing at least one differentiated antigen presenting cell (APC), the method comprising: culturing a population of peripheral blood or bone marrow mononuclear cells in interleukin-4 (IL-4), granulocyte macrophage colony stimulating factor (GM-CSF), and a culture medium comprising insulin, transferrin, linoleic acid, oleic acid, and palmitic acid for a sufficient time to produce the at least one differentiated antigen presenting cell.

2. (Amended) The method of claim 1, wherein the at least one differentiated APC comprises a dendritic cell.

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5. (Amended) The method of claim 4, wherein the dendritic cell comprises an mDC2.

6. (Amended) The method of claim 2, wherein the dendritic cell comprises a dendritic cell comprising one or more of the following characteristics: expresses substantially less CD1a on its surface, produces substantially less IL-12, produce substantially a increased amount of IL-10, and induces or promotes T cell differentiation to Th0 or Th2 subtype, as compared to a dendritic cell produced by culturing a population of peripheral blood or bone marrow mononuclear cells in IL-4, GM-CSF, and a culture medium comprising RPMI.

7. (Amended) The method of claim 2, wherein the dendritic cell is capable of presenting at least one antigen to a T cell.

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10. (Amended) The method of claim 9, further comprising depleting the population of mononuclear cells with immunomagnetic beads.

11. (Amended) The method of claim 1, further comprising deriving the population of mononuclear cells by density gradient separation of standard buffy coat preparations of peripheral blood.

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13. (Amended) The method of claim 12, further comprising depleting the population of mononuclear cells with immunomagnetic beads.

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17. (Amended) The method of claim 15, wherein the differentiated APC comprises a dendritic cell.

18. (Amended) The method of claim 17, wherein the dendritic cell substantially lacks IL-12 production compared to a dendritic cell produced by culturing a population of peripheral blood or bone marrow mononuclear cells in IL-4, GM-CSF, and a culture medium comprising RPMI.

19. (Amended) The method of claim 17, wherein the dendritic cell has

substantially increased IL-10 production as compared to a dendritic cell produced by culturing a population of peripheral blood or bone marrow mononuclear cells in IL-4, GM-CSF, and a culture medium comprising RPMI.

20. (Amended) The method of claim 2 or 17, wherein the dendritic cell induces or promotes Th0 and/or Th2 differentiation of T cells or substantially lacks expression of CD1a cell surface marker.

23. (Amended) The method of claim 21, wherein the differentiated APC comprises a dendritic cell.

24. (Amended) The method of claim 23, wherein the dendritic cell comprises a dendritic cell that substantially lacks expression of CD1a cell surface marker.

25. (Amended) The method of claim 23, wherein the dendritic cell substantially lacks IL-12 production or induces or promotes differentiation of T cells to Th0/Th2, as compared to a dendritic cell produced by culturing a population of peripheral blood or bone marrow mononuclear cells in IL-4, GM-CSF, and a culture medium comprising RPMI.

27. (Amended) The method of claim 23, wherein the dendritic cell comprises one or more of the following characteristics: substantially lacks expression of CD1a cell surface marker, substantially lacks IL-12 production, exhibits increased IL-10 production, and induces or promotes Th0/Th2 differentiation of T cells, as compared to a dendritic cell produced by culturing a population of peripheral blood or bone marrow mononuclear cells in IL-4, GM-CSF, and a culture medium comprising RPMI.

28. (Amended) The method of claim 21, further comprising culturing the APC in the presence of an anti-CD40 monoclonal antibody for a period of approximately 24 hours, thereby providing an activated APC; and culturing the activated APC in the presence of lipopolysaccharide (LPS) and interferon-gamma (IFN-g) for a period of approximately 48 hours, thereby producing a mature CD83<sup>+</sup> dendritic cell.

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29. (Amended) The method of claim 28, wherein the CD83<sup>+</sup> dendritic cell comprises one or more of the following characteristics: substantially lacks production of IL-12, exhibits increased IL-10 production, substantially lacks expression of CD1a cell surface marker, and induces or promotes Th0 or Th2 differentiation of T cell, as compared to a dendritic cell produced by culturing a population of peripheral blood or bone marrow mononuclear cells in IL-4, GM-CSF, and a culture medium comprising RPMI.

30. (Amended) The method of claim 2 or 24, further comprising introducing to at least one dendritic cell at least one exogenous DNA sequence operably linked to a promoter that is capable of controlling expression of said DNA sequence, which at least one exogenous DNA sequence encodes at least one antigen, in an amount sufficient that expression and presentation of the at least one antigen results, thereby producing an antigen presenting dendritic cell.

31. (Amended) The method of claim 30, further comprising introducing said at least one exogenous DNA sequence to at least one dendritic cell by a method selected from electroporation, injection, microinjection, gene gun delivery, lipofection, DOTAP supplemented lipofection, DOSPER supplemented lipofection, or Superfection.

32. (Amended) The method of claim 2 or 24, further comprising introducing a sufficient amount of at least one antigen or antigenic fragment thereof to at least one dendritic cell, such that presentation of the at least one antigen on least one dendritic cell occurs, thereby producing an antigen presenting dendritic cell.

33. (Amended) A differentiated antigen presenting cell (APC), which differentiated APC expresses substantially less CD1a cell surface marker than a conventional dendritic cell.

34. (Amended) The differentiated APC of claim 33, wherein said differentiated APC comprises a monocyte-derived dendritic cell.

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35. (Amended) The differentiated APC of claim 34, wherein monocyte-derived dendritic cell comprises one or more of the following characteristics: substantially lacks IL-12 production, induces or promotes Th0 or Th2 T cell differentiation, and exhibits increased IL-10 production, as compared to a conventional dendritic cell.

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39. (Amended) The differentiated APC of claim 37, wherein the monocyte-derived dendritic cell comprises one or more of the following characteristics: substantially lacks IL-12 production, induces or promotes Th0 or Th2 T cell differentiation, substantially lacks CD1a surface marker expression, and exhibits substantially increased IL-10 production, as compared to a dendritic cell produced by culturing a population of peripheral blood or bone marrow mononuclear cells in IL-4, GM-CSF, and a culture medium comprising RPMI.

41. (Amended) The differentiated APC of claim 37, wherein the monocyte-derived dendritic cell has a transfection efficiency greater than that of a dendritic cell produced by culturing a population of monocytes in IL-4, GM-CSF, and a culture medium comprising RPMI.

42. (Amended) A method of inducing in a subject an immune response to at least one antigen, said method comprising administering to the subject a population of dendritic cells, said dendritic cells displaying or presenting at least one of said at least one antigen, in an

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amount sufficient to induce the immune response to said at least one antigen, said dendritic cells comprising one or more of the following characteristics: substantially lacking IL-12 production, inducing or promoting T cell differentiation to a Th0 or Th2 subtype, substantially lacking CD1a surface marker expression, and substantially increasing IL-10 production, as compared to a conventional dendritic cell.

Please cancel claim 43 without prejudice to subsequent renewal.

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44. (Amended) The method of claim 42, wherein said dendritic cell is produced by culturing a population of peripheral blood or bone marrow mononuclear cells in interleukin-4 (IL-4), granulocyte macrophage colony stimulating factor (GM-CSF), and a culture medium comprising insulin, transferrin, linoleic acid, oleic acid, palmitic acid for a sufficient time to produce the differentiated antigen presenting cell.

46. (Amended) A method of inducing differentiation of T cells, the method comprising: co-culturing a population of T cells with a population of antigen presenting cells (APC) that substantially lacks CD1a expression, thereby inducing or promoting differentiation of said T cells.

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48. (Amended) The method of claim 46, wherein the antigen presenting cells that substantially lack CD1a expression comprise dendritic cells.

49. (Amended) The method of claim 48, wherein the dendritic cells produce substantially no IL-12, as compared to conventional dendritic cells.

50. (Amended) The method of claim 48, wherein the dendritic cells produce substantially no IL-12 compared to dendritic cells produced by culturing a population of peripheral blood or bone marrow mononuclear cells in IL-4, GM-CSF, and a culture medium comprising RPMI.

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52. (Amended) A composition comprising a population of dendritic cells, said dendritic cells comprising at least one of the following characteristics: substantially lacking

interleukin-12 (IL-12) production, substantially lacking CD1a surface marker expression, exhibiting increased IL-10 production, and inducing or promoting T cell differentiation to Th0 or Th2 subtype, as compared to a conventional dendritic cell.

53. (Amended) The composition of claim 52, wherein said dendritic cells are capable of presenting an antigen to a T cell.

54. (Amended) The composition of claim 52, wherein said dendritic cells produce substantially less or no IL-12 and express substantially less CD1a surface marker, as compared to conventional dendritic cells.

55. (Amended) The composition of claim 52, wherein said dendritic cells promote differentiation of T cells to a Th0/Th2 subtype and produce substantially less IL-12, as compared to conventional dendritic cells.

56. (Amended) The composition of claim 52, wherein said dendritic cells display or present at least one antigen or antigenic fragment thereof.

57. (Amended) The composition of claim 56, wherein the at least one antigen or antigenic fragment comprises a protein or peptide derived from a protein or peptide that is differentially expressed on a cell selected from the group consisting of a tumor cell, a bacterially-infected cell, a parasitically-infected cell, a virally-infected cell, and a target cell of an autoimmune response.

60. (Amended) A method of inducing or modulating an immune response in an immunocompromised subject, said method comprising administering to the subject a population of dendritic cells in an amount sufficient to induce or modulate an immune response in the subject, said dendritic cells exhibiting one or more of the following characteristics: substantially lacking interleukin-12 (IL-12) production, substantially lacking expression of CD1a surface marker, exhibiting increased IL-10 production, and inducing or promoting differentiation of T cells to Th0 or Th2 subtype, as compared to conventional dendritic cells.

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61. (Amended) An ex vivo method of inducing in a subject a therapeutic or prophylactic immune response against at least one antigen, the method comprising:

a) culturing a population of monocytes obtained from the subject with IL-4, GM-CSF, and a culture medium comprising Iscove's Modified Dulbecco's Medium (IMDM) supplemented with insulin, transferrin, linoleic acid, oleic acid and palmitic acid for a sufficient time to produce a population of dendritic cells;

b) introducing to the population of dendritic cells a sufficient amount of at least one antigen, or a sufficient amount of an exogenous DNA sequence operably linked to a promoter that controls expression of said DNA sequence, said DNA sequence encoding at least one or said at least one antigen, such that the presentation of the antigen on the dendritic cells results; and

c) administering the antigen-presenting dendritic cells to the subject in an amount sufficient to induce a therapeutic or prophylactic immune response against said at least one antigen.

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63. (Amended) A method for therapeutically or prophylactically treating a disease in a subject in need of treatment of said disease, the method comprising:

a) culturing a population of monocytes obtained from the subject with IL-4, GM-CSF, and a culture medium comprising Iscove's Modified Dulbecco's Medium (IMDM) supplemented with insulin, transferrin, linoleic acid, oleic acid and palmitic acid for a sufficient time to produce a population of dendritic cells;

b) introducing to the population of dendritic cells a sufficient amount of at least one disease-associated antigen, or a sufficient amount of an exogenous DNA sequence operably linked to a promoter that controls expression of said DNA sequence, said DNA sequence encoding at least one of said at least one disease-associated antigen, such that presentation of the disease-associated antigen on the dendritic cells results; and

c) administering a therapeutic or prophylactic amount of the dendritic cells presenting the disease-associated antigen to the subject to treat said disease.



Q32 65. (Amended) A method for therapeutically or prophylactically treating a disease in a subject in need of treatment of the disease, the method comprising:

a) culturing a population of monocytes obtained from the subject with IL-4, GM-CSF, and a culture medium comprising Iscove's Modified Dulbecco's Medium (IMDM) supplemented with insulin, transferrin, linoleic acid, oleic acid and palmitic acid for a sufficient time to produce a population of dendritic cells;

b) contacting the population of dendritic cells with a population of diseased cells from a tissue or organ of the subject, thereby inducing presentation of a disease-associated antigen on the dendritic cells; and

c) administering a therapeutic or prophylactic amount of dendritic cells presenting the disease-associated antigen to the subject to treat the disease.

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Q33 68. (Amended) A monocyte-derived dendritic cell, wherein the dendritic cell comprises one or more of the following characteristics: does not substantially express CD1a cell marker, substantially lacks IL-12 production, exhibits increased IL-10 production, and promotes Th0 and/or Th1 lineage differentiation of T cells.

Please cancel claim 69 without prejudice to subsequent renewal.

Please add new claims 70-78 as follows.

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Q34 70. (New) A population of monocyte-derived dendritic cells produced by culturing a population of monocyte cells in interleukin-4 (IL-4), granulocyte macrophage colony stimulating factor (GM-CSF), and a culture medium comprising insulin, transferrin, linoleic acid, oleic acid, and palmitic acid, wherein the monocyte-derived dendritic cells comprising an altered cytokine profile compared to dendritic cells produced by culturing a population of monocyte cells in IL-4, GM-CSF, and a culture medium comprising RPMI.

71. (New) The population of monocyte-derived dendritic cells of claim 69, wherein said monocyte-derived dendritic cells comprise one or more of the following

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characteristics: produce substantially less interleukin-12 (IL-12), produce substantially more IL-10, express less CD1a cell surface marker, and induce or promote increased T cell differentiation to Th0 or Th2 subtype, as compared to a population of dendritic cells produced by culturing a population of monocyte cells in IL-4, GM-CSF, and a culture medium comprising RPMI.

72. (New) A population of dendritic cells produced by culturing a population of peripheral blood or bone marrow mononuclear cells in interleukin-4 (IL-4), granulocyte macrophage colony stimulating factor (GM-CSF), and Yssel's culture medium, wherein said dendritic cells exhibit one or more of the following characteristics:  
substantially lack interleukin-12 (IL-12) production, express less CD1a cell surface marker, induce or promote increased T cell differentiation to Th0 or Th2 subtype, exhibit substantially increased IL-10 production, as compared to dendritic cells produced by culturing a population of monocyte cells in IL-4, GM-CSF, and a culture medium comprising RPMI.

73. (New) A vaccine composition comprising at least one dendritic cell, wherein said at least one dendritic cell comprises one or more of the following characteristics: produce substantially less interleukin-12 (IL-12), produce substantially more IL-10, express substantially less CD1a cell surface marker, and induce or promote increased T cell differentiation to Th0 or Th2 subtype, as compared to a conventional dendritic cell.

74. (New) The vaccine composition of claim 73, wherein the at least one dendritic cell displays or presents at least one antigen or immunogenic peptide on its surface.

75. (New) The vaccine composition of claim 73, further comprising a pharmaceutically acceptable carrier or an adjuvant.

76. (New) The vaccine composition of claim 73, wherein said vaccine composition is useful for prophylactic or therapeutic treatment of cancer.

77. (New) The method of claim 2, wherein the dendritic cell substantially lacks expression of CD1a cell surface marker.

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